

AMENDMENTS

In the Claims:

1. (Currently Amended) A method for detecting whether a subject has is suffering from or is predisposed to developing a disease or condition that is associated with an IL-1 inflammatory haplotype, comprising detecting a plurality of one or more alleles from an IL-1 inflammatory haplotype selected from the group consisting of: an IL-1 44112332 inflammatory haplotype, and an IL-1 33441461 inflammatory haplotype allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN, wherein the presence of the plurality of said one or more alleles indicates that the subject is predisposed to the development of or has the disease or condition.
2. (Original) A method of claim 1, wherein the disease or condition is selected from the group consisting of an inflammatory disease, a degenerative disease an immunological disorder, an infectious disease, a trauma induced disease, and a cancer.
3. (Original) A method of claim 1, wherein said detecting step is selected from the group consisting of:
 - a) allele specific oligonucleotide hybridization;
 - b) size analysis;
 - c) sequencing;
 - d) hybridization;
 - e) 5' nuclease digestion;
 - f) single-stranded conformation polymorphism;
 - g) allele specific hybridization;
 - h) primer specific extension; and
 - j) oligonucleotide ligation assay.

4. (Original) A method of claim 1, wherein prior to or in conjunction with detection, the nucleic acid sample is subject to an amplification step.
5. (Original) A method of claim 4, wherein said amplification step employs a primer selected from the group consisting of any of SEQ ID Nos.8-32.
6. (Original) A method of claim 3, wherein said size analysis is preceded by a restriction enzyme digestion.
7. (Cancelled)
8. (Currently Amended) A method for selecting an appropriate therapeutic for an individual that has is suffering from or is predisposed to developing a disease or disorder that is associated with an IL-1 polymorphism, comprising the steps of: detecting a plurality of one or more alleles from an IL-1 inflammatory haplotype selected from the group consisting of: an IL-1 44112332 inflammatory haplotype, and an IL-1 33441461 inflammatory haplotype allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN, and selecting a therapeutic that compensates for a causative functional mutation that is in linkage disequilibrium with the IL-1 alleles.
9. (Original) A method of claim 8, wherein said detecting is performed using a technique selected from the group consisting of:
 - a) allele specific oligonucleotide hybridization;
 - b) size analysis;
 - c) sequencing;
 - d) hybridization;
 - e) 5' nuclease digestion;
 - f) single-stranded conformation polymorphism;
 - g) allele specific hybridization;
 - h) primer specific extension; and

j) oligonucleotide ligation assay.

10. (Original) A method of claim 8, wherein prior to or in conjunction with detecting, the nucleic acid sample is subjected to an amplification step.
11. (Original) A method of claim 10, wherein said amplification step employs a primer selected from the group consisting of SEQ ID Nos. 8-32.
12. (Original) A method of claim 9, wherein said size analysis is preceded by a restriction enzyme digestion.
13. (Currently Amended) A method of claim 9, wherein the disease or condition is selected from the group consisting of: an inflammatory disease, a degenerative disease an immunological disorder, an infectious disease, a trauma induced disease, and a cancer.
14. (Original) A method of claim 9, wherein the therapeutic is a modulator of an IL-1 activity.
15. (Original) A method of claim 14, wherein the IL-1 activity is IL-1 α .
16. (Original) A method of claim 14, wherein the IL-1 activity is IL-1 β .
17. (Original) A method of claim 14, wherein the IL-1 activity is IL-1RN.
18. (Original) A method of claim 14, wherein the modulator of an IL-1 activity is a protein, peptide, peptidomimetic, small molecule, nucleic acid or a nutraceutical.
19. (Original) A method of claim 14, wherein the modulator is an agonist.
20. (Original) A method of claim 14, wherein the modulator is an antagonist.
21. - 28 (Cancelled)
29. (Currently Amended) A method for treating or preventing the development of a disease or condition that is associated with an IL-1 polymorphism in a subject comprising the steps of: detecting a plurality of one or more alleles from an IL-1 inflammatory haplotype selected from the group consisting of: an IL-1 44112332 inflammatory haplotype, and an IL-1 33441461 inflammatory haplotype allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker

of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN; and administering to the subject a therapeutic that compensates for a causative mutation that is in linkage disequilibrium with the IL-1 inflammatory haplotype.

30. (Original) A method of claim 29, wherein the detecting step is selected from the group consisting of:

- a) allele specific oligonucleotide hybridization;
- b) size analysis;
- c) sequencing;
- d) hybridization;
- e) 5' nuclease digestion;
- f) single-stranded conformation polymorphism;
- g) allele specific hybridization;
- h) primer specific extension; and
- j) oligonucleotide ligation assay.

31. (Original) A method of claim 29, wherein prior to or in conjunction with detecting, the nucleic acid sample is subjected to an amplification step.

32. (Original) A method of claim 29, wherein said amplification step employs a primer selected from the group consisting of any of SEQ ID Nos. 8-32.

33. (Original) A method of claim 30, wherein said size analysis is preceded by a restriction enzyme digestion.

34. (Original) A method of claim 30, wherein the therapeutic is selected from the group consisting of: a modulator of an IL-1 activity.

35. (Original) A method of claim 34, wherein the IL-1 activity is IL-1 α .

36. (Original) A method of claim 34, wherein the IL-1 activity is IL-1 β .

37. (Original) A method of claim 34, wherein the IL-1 activity is IL-1Ra.
38. (Original) A method of claim 34, wherein the therapeutic is a protein, peptide, peptidomimetic, small molecule or a nucleic acid.
39. (Original) A method of claim 34, wherein the modulator is an agonist.
40. (Original) A method of claim 34, wherein the modulator is an antagonist.
- 41.- 57. (Cancelled)
58. (New) The method of claim 1, further comprising detecting allele 2 of the VNTR marker of IL-1RN.
59. (New) The method of claim 8, further comprising detecting allele 2 of the VNTR marker of IL-1RN.
60. (New) The method of claim 29, further comprising detecting allele 2 of the VNTR marker of IL-1RN.
61. (New) A method for detecting whether a subject is suffering from or is predisposed to developing a cardiovascular disease, comprising detecting one or more alleles selected from the group consisting of: allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN, wherein the presence of said one or more alleles indicates that the subject is predisposed to the development of or has a cardiovascular disease.
62. (New) A method for detecting whether a subject is suffering from or is predisposed to developing osteoporosis, comprising detecting one or more alleles selected from the group consisting of: allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker,

allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN, wherein the presence of said one or more alleles indicates that the subject is predisposed to the development of or has osteoporosis.

63. (New) A method for selecting an appropriate therapeutic for an individual that is suffering from or is predisposed to developing a cardiovascular disease, comprising the steps of: detecting one or more alleles selected from the group consisting of: allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN, and selecting a therapeutic that compensates for a causative functional mutation that is in linkage disequilibrium with the IL-1 alleles.

64. (New) A method for selecting an appropriate therapeutic for an individual that is suffering from or is predisposed to developing osteoporosis, comprising the steps of: detecting one or more alleles selected from the group consisting of: allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN, and selecting a therapeutic that compensates for a causative functional mutation that is in linkage disequilibrium with the IL-1 alleles.

65. (New) A method for treating or preventing the development of a cardiovascular disease in a subject comprising the steps of: detecting one or more alleles selected from the group

consisting of: allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN; and administering to the subject a therapeutic that compensates for a causative mutation that is in linkage disequilibrium with the IL-1 inflammatory haplotype.

66. (New) A method for treating or preventing the development of osteoporosis in a subject comprising the steps of: detecting one or more alleles selected from the group consisting of: allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN; and administering to the subject a therapeutic that compensates for a causative mutation that is in linkage disequilibrium with the IL-1 inflammatory haplotype.